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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/618,170	07/18/00	LINCOLN	S 13020-11

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DAVID A KALOW
KALOW & SPRINGUT LLP
19TH FLOOR
488 MADISON AVENUE
NEW YORK NY 10022

EXAMINER	
FRIEDMAN, J	
ART UNIT	**PAPER NUMBER**
1655	4

DATE MAILED: 06/13/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/618,178	Lincoln et al
Examiner	**Art Unit**
Jeffrey Fredman	1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Mar 15, 2001* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *48-71* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *48-71* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Priority

1. Applicant's claim of priority back to application 08/173,173, 07/775,786 and 07/664,837 is noted. The examiner was unable to determine whether these applications provide support for the entirety of the current claims and therefore the claims are given the effective date of the immediate parent 09/088,820, which provides express support (except for claim 50, as detailed below).

Claim Rejections - 35 USC § 112

2. Claim 50 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

With regard to new matter issues, MPEP 2163.03 notes "An amendment to the claims or the addition of a new claim must be supported by the description of the invention in the application as filed. In re Wright , 866 F.2d 422, 9 USPQ2d 1649 (Fed. Cir. 1989)". MPEP 2163.04 notes "the examiner has the initial burden of presenting evidence or reasoning to explain why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims."

The specific new limitation is that "the Euclidean representation is a two dimensional plot of a first reaction value on the x-axis and a second reaction value on the y-axis (claim 50)".

The specification does not discuss any plots associated with the Euclidean representation and the specification gives no basis for a two dimensional plot. The only basis for any dimension in the specification is an "m-dimensional representation (page 12, line 23)". Further, there is no correlation or discussion of "reaction values (claim 50)" in any way associated with the euclidean represenation. Therefore, the term as discussed in claim 50 appears to represent new matter.

3. Claims 48-68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is vague and indefinite what is meant by "Euclidean representation" for two reasons.

First, the specification at page 12 as indicated in the Applicant's preliminary amendment gives no definition of this term. Second, the claim lacks any definition or clarification of the term. Therefore, since it is unclear what constitutes a Euclidean representation, the rejection of the parent application remains applicable. With regard to claims 69-71, which lack the Euclidean limitation, the Kimpton rejection also, of course, remains applicable.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> > (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

5. Claims 48-55 and 69-71 are rejected under 35 U.S.C. 102(a) as being anticipated by Kimpton et al (PCR Meth. Appl. (August 1993) 3:13-22).

Kimpton teaches a method of determining the genotype at a locus within genetic material obtained by PCR amplification (page 14) comprising:

a) reacting the material at the locus to produce a first reaction value indicative of the presence of the given allele at the locus (page 14 and page 15, figure 1),

b) forming a data set including the first reaction value (page 15, figure 1 and column 1).

c) establishing a plurality of distribution sets of probability distributions where hypothetic reaction values are associated with each genotype of interest at the locus (page 15, column 1 and page 16, columns 1 and 2),

d) applying the first reaction value to teach pertinant probability distribution to determine a measure of the conditional probability of each genotype at the locus (page 16, columns 2 and 3),

e) determining the genotype based on the data obtained from step d) (page 16 and page 17).

Kimpton expressly teaches reacting the material at multiple loci (page 14, table 1). On page 17, Kimpton expressly considers multiple alleles in the probability distributions, particularly in table 2 which expressly notes that the method is applicable to any number of alleles. Kimpton expressly teaches the use of multiple data points derived from multiple runs of the automated apparatus including multiple data sets in the exemplified method and apparatus (page 16, especially figure 2). Kimpton expressly teaches that the locus may be dinucleotide or

tetranucleotide repeats (page 13). Kimpton expressly selected the loci for their discrimination ability (page 16, column 1).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 48-55 and 60-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kimpton in view of Clark et al (Mol. Biol. Evol. (March 1990) 7(2):111-122).

Kimpton teaches the methods of claims 48-55 as discussed above. Kimpton does not teach modification of the data to iteratively improve the assay.

Clark teaches a method of resolving ambiguities by performing an iterative cascade of improvements on the data points (abstract and pages 111-113). Clark also applies the method to restriction site polymorphisms.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the iterative screening and improvement methods of Clark with the probability method of Kimpton since Clark states "Details of the algorithm for extracting allellic sequences are presented here, along with some population genetic considerations that influence the likelihood of success of the method. The algorithm also applies to the problem of inferring haplotype frequencies of closely linked restriction site polymorphisms (abstract)". An ordinary practitioner would have been motivated to apply the conceptual idea of iterative data processing of Clark in the genotyping method of Kimpton in order to extract the as close to the entirety of the allelic sequences as possible. Further, an ordinary practitioner would have recognized that the method could be performed using any length marker, including single nucleotide polymorphisms such as the restriction site polymorphisms expressly discussed and motivated by Clark.

8. Claims 48-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kimpton in view of Clark and further in view of Goelet et al (WO 92/15712).

Kimpton in view of Clark teaches the methods of claims 48-55 and 60-69 as discussed above. Kimpton in view of Clark does not teach genetic bit analysis, which includes allele specific amplification.

Goelet teaches genetic bit analysis methods, including allele specific amplification methods (see entire document, expecially pages 10-13).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the method of Kimpton in view of Clark with the use of genetic bit analysis or allele specific amplification to develop the data since Goelet states "The current invention provides a method that can be used to diagnose or characterize nucleic acids in biological samples without recourse to gel electrophoretic size separation of the nucleic acid species. This feature renders this process easily adaptable to automation and thus will permit the analysis of large numbers of samples at relatively low cost (page 8, lines 27-33)". An ordinary practitioner would have been motivated to substitute the equivalent genetic bit analysis method for PCR in order to minimize the need for gel electrophoresis and enhance the automatability of the process as expressly motivated by Goulet in order to speed analysis and minimize costs.

9. Claims 48-56, 58 and 60-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kimpton in view of Clark and further in view of Backman et al (U.S. Patent 5,516,663).

Kimpton in view of Clark teaches the methods of claims 48-55, 60-69 as discussed above. Kimpton in view of Clark does not the use of ligation chain reaction.

Backman teaches a method of LCR (abstract).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the method of Kimpton in view of Clark with the use of LCR as taught by Backman since Backman states "One of the great strengths of amplification reactions

is their ability to detect exceedingly small numbers of target molecules (column 2, lines 8-10)". An ordinary practitioner would have been motivated to substitute LCR for the equivalent amplification method of PCR for the express motivation that LCR can detect small numbers of target molecules and because LCR is a known equivalent amplification assay to the PCR used by Kimpton.

Conclusion

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeff Fredman, Ph.D. whose telephone number is (703) 308-6568. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission via the P.T.O. Fax Center located in Crystal Mall 1. The CM1 Fax Center numbers for Technology Center 1600 are either (703) 305-3014 or (703) 308-4242. Please note that the faxing of such papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Jeffrey Fredman
Primary Patent Examiner
Art Unit 1655

June 12, 2001